

DOCKET NO.: ISPH-0519

PATENT

## A S S I G N M E N T

WHEREAS, We, Brett P. Monia, of La Costa, State of California; Lex M. Cowser, of Carlsbad, State of California, Susan Murray, of Poway, State of California, Madeline M. Butler, of Rancho Santa Fe, State of California; and Nicholas M. Dean, of Olivenhain, State of California, have invented a certain invention entitled Antisense Modulation of PI3K P85 Expression, for which we have made application for Letters Patent of the United States, said application having been filed November 20, 2000 and assigned Application No. 09/715,983; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all

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countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any

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and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

DATED: 2/1, 2001

Brett P. Monia  
BRETT P. MONIA

State of California       )  
                                  ) ss.  
County of San Diego       )

On this 1<sup>st</sup> day of February, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Brett P. Monia, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

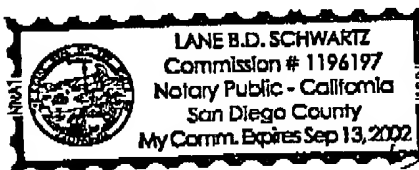
[Signature]  
Signature of Notary

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DATED: 1/31/01, 2001  
LEX M. COWSERTState of California )  
County of San Diego ) ss.

On this 31<sup>st</sup> day of January, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Lex M. Cowsert, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



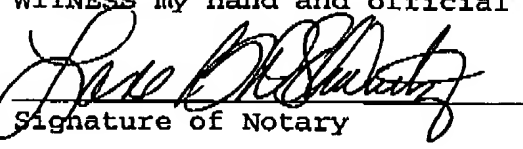
WITNESS my hand and official seal.

  
Signature of NotaryDATED: 1/19, 2001  
SUSAN MURRAYState of California )  
County of San Diego ) ss.

On this 19<sup>th</sup> day of January, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Susan Murray, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

  
Signature of Notary

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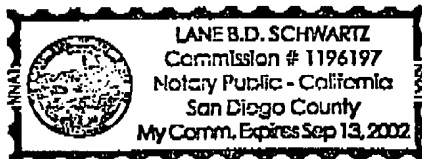
DATED: Jan 31, 2001

Madeline M. Butler  
 MADELINE M. BUTLER

State of California )  
 ) ss.  
 County of San Diego )

On this 31<sup>st</sup> day of January, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Madeline M. Butler, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.



Lane B.D. Schwartz  
 Signature of Notary

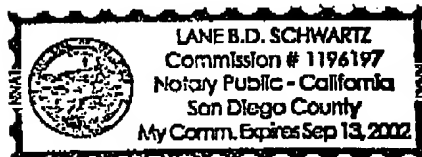
DATED: 1/30, 2001

Nicholas M. Dean  
 NICHOLAS M. DEAN

State of California )  
 ) ss.  
 County of San Diego )

On this 30<sup>th</sup> day of January, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Nicholas M. Dean, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.



Lane B.D. Schwartz  
 Signature of Notary

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Table A

Serial No. Patent No. Docket No.	Filing Date Issue Date	Inventor(s)	Examiner	Art Unit	Title
09/577,902 6,284,538 ISIS0004-102	May 24, 2000 September 4, 2001	B. Monia et al.	M. Schmidt	1635	ANTISENSE INHIBITION OF PTEN EXPRESSION
09/048,810 6,238,921 ISIS0052-101	March 26, 1998 May 29, 2001	L. Miraglia et al.	M. Shibuya	1635	ANTISENSE OLIGONUCLEOTIDE MODULATION OF HUMAN MDM2 EXPRESSION
09/280,805 6,184,212 ISIS0052-102	March 26, 1999 February 6, 2001	L. Miraglia et al.	J. Epps	1635	ANTISENSE MODULATION OF HUMAN MDM2 EXPRESSION
09/731,457 ISIS0053-100	December 6, 2000	I. Popoff et al.	J. Schultz	1635	ANTISENSE MODULATION OF DAMAGE SPECIFIC DNA BINDING PROTEIN 1, P127 EXPRESSION
09/659,860 ISIS0054-100	September 11, 2000	H. Zhang et al.	J. Schultz	1635	ANTISENSE MODULATION OF CASPASE 7 EXPRESSION
10/007,078 ISIS0055-100	November 8, 2001	D. Ward et al.	J. Schultz	1635	ANTISENSE MODULATION OF EIF2C1 EXPRESSION
09/953,611 ISIS0056-100	September 13, 2001	D. Ward et al.	To Be Determined	1635	ANTISENSE MODULATION OF PROTEIN KINASE R EXPRESSION
09/715,983 ISIS0057-100	November 20, 2000	B. Morita et al.	J. Zara	1635	ANTISENSE MODULATION OF PI3K P85 EXPRESSION
09/344,521 6,100,090 ISIS0057-101	June 25, 1999 August 8, 2000	B. Monia et al.	J. Zara	1635	ANTISENSE INHIBITION OF PI3K P85 EXPRESSION
09/954,679 ISIS0058-100	September 12, 2001	D. Ward et al.	K. Lacourciere	1635	ANTISENSE MODULATION OF RIBONUCLEASE L EXPRESSION
09/484,617 6,303,374 ISIS0059-100	January 18, 2000 October 16, 2001	H. Zhang et al.	S. McGarry	1635	ANTISENSE MODULATION OF CASPASE 3 EXPRESSION

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Serial No. Patent No. Docket No.	Filing Date Issue Date	Inventor(s)	Examiner	Art Unit	Title
09/679,298 6,566,131 ISIS0060-100	October 4, 2000 May 20, 2003	L. Cowser	M. Schmidt	1635	ANTISENSE MODULATION OF SMAD6 EXPRESSION
09/679,299 6,566,135 ISIS0061-100	October 4, 2000 May 20, 2003	A. Watt	J. Zara	1635	ANTISENSE MODULATION OF CASPASE 6 EXPRESSION
09/853,768 6,444,466 ISIS0062-100	May 10, 2001 September 3, 2002	D. Ward et al.	J. LeGuyader	1635	ANTISENSE MODULATION OF HELICASE- MOI EXPRESSION
10/001,863 ISIS0063-100	November 19, 2001	J. Karras et al.	To Be Determined	1645	ANTISENSE MODULATION OF TOLL-LIKE RECEPTOR 4 EXPRESSION
09/865,993 ISIS0064-100	May 25, 2001	B. Monia et al.	J. Zara	1635	ANTISENSE MODULATION OF DUAL SPECIFIC PHOSPHATASE 5 EXPRESSION
09/667,018 ISIS0065-100	September 20, 2000	H. Zhang et al.	J. Schultz	1635	ANTISENSE MODULATION OF CASPASE 2 EXPRESSION
10/271,887 ISIS0066-100	October 15, 2002	H. Zhang et al.	To Be Determined	1635	ANTISENSE MODULATION OF CASPASE 9 EXPRESSION
09/659,845 6,492,170 ISIS0066-101	September 11, 2000 December 10, 2002	A. Watt	A. Wang	1639	ANTISENSE MODULATION OF CASPASE 9 EXPRESSION
10/309,362 ISIS0067-100	December 3, 2002	D. Ward et al.	To Be Determined	1635	ANTISENSE MODULATION OF RECQL5 EXPRESSION
10/238,443 ISIS0067-101	September 9, 2002	D. Ward et al.	To Be Determined	1635	ANTISENSE MODULATION OF RECQL5 EXPRESSION
09/798,185 ISIS0067-102	March 1, 2001	D. Ward et al.	K. Lacourciere	1635	ANTISENSE MODULATION OF RECQL5 EXPRESSION
09/798,096 6,399,378 ISIS0068-100	March 1, 2001 June 4, 2002	D. Ward et al.	S. McGarry	1635	ANTISENSE MODULATION OF RECQL2 EXPRESSION

Serial No. Patent No. Docket No.	Filing Date Issue Date	Inventor(s)	Examiner	Art Unit	Title
09/792,594 6,436,706 ISIS0069-100	February 23, 2001 August 20, 2002	D. Ward et al.	K. Lacourciere	1635	ANTISENSE MODULATION OF RECQL4 EXPRESSION
09/793,807 ISIS0070-100	February 23, 2001	D. Ward et al.	J. Zara	1635	ANTISENSE MODULATION OF RECQL EXPRESSION
09/358,381 6,020,199 ISIS0071-100	July 21, 1999 February 1, 2000	B. Morita et al.	M. Schmidt	1635	ANTISENSE MODULATION OF PTEN EXPRESSION
10/006,430 ISIS0072-100	December 10, 2001	M. Graham et al.	S. McGarry	1635	ANTISENSE MODULATION OF CD81 EXPRESSION
10/175,492 ISIS0073-100	June 17, 2002	K. Dobie et al.	To Be Determined	1645	ANTISENSE MODULATION OF PAZ/PIWI DOMAIN CONTAINING PROTEIN EXPRESSION
10/199,221 ISIS0074-100	July 18, 2002	B. Morita et al.	J. Epps	1635	ANTISENSE MODULATION OF DUAL SPECIFIC PHOSPHATASE 6 EXPRESSION
09/487,444 6,159,697 ISIS0075-100	January 19, 2000 December 12, 2000	B. Morita et al.	A. Wang	1635	ANTISENSE MODULATION OF SMAD7 EXPRESSION
10/181,603 ISIS0075-101	July 17, 2002	B. Morita et al.	To Be Determined	1651	ANTISENSE MODULATION OF SMAD7 EXPRESSION
09/732,199 6,379,960 ISIS0076-100	December 6, 2000 April 30, 2002	I. Popoff et al.	M. Schmidt	1635	ANTISENSE MODULATION OF DAMAGE- SPECIFIC DNA BINDING PROTEIN 2, p48 EXPRESSION
09/920,668 6,482,844 ISIS0077-100	August 1, 2001 November 19, 2002	L. Cowsett	M. Schmidt	1635	ANTISENSE MODULATION OF DUAL SPECIFIC PHOSPHATASE 8 EXPRESSION
09/922,146 6,566,133 ISIS0078-100	August 1, 2001 May 20, 2003	L. Cowsett	T. Gibbs	1635	ANTISENSE MODULATION OF DUAL SPECIFIC PHOSPHATASE 9 EXPRESSION



Serial No., Patent No., Docket No.	Filing Date Issue Date	Inventor(s)	Examiner	Art Unit	Title
09/487,445 6,258,600 ISIS0079-100	January 19, 2000 July 10, 2001	H. Zhang et al.	M. Shibuya	1635	ANTISENSE MODULATION OF CASPASE 8 EXPRESSION
10/181,177 ISIS0079-101	July 12, 2002	H. Zhang et al.	To Be Determined	1632	ANTISENSE MODULATION OF CASPASE 8 EXPRESSION